Remarks

Introduction

Claims 22 to 65 are pending in this case. Claims 22-36 and 59-65 are herewith canceled as being directed to non-elected subject matter. Additionally, applicants herewith cancel claims 44, 45, 46, 48, and 50, without prejudice or disclaimer. Thus, with entry of this amendment, claims 37-43, 47, 49 and 50-58 will be pending and active in this case.

Receipt is acknowledged of the Final Office Action dated February 11, 2002. In the Action, the Examiner has maintained the rejection of claims 37-58 under 35 U.S.C. § 112, first paragraph as allegedly non-enabled.

Applicants respond to the above rejection in line with suggestions made during the interview of April 23, 2002. Applicants thank Examiner Hunt for the opportunity for that interview and for her guidance.

A marked-up copy of the claims, as amended, is attached. Applicants believe that entry of this amendment is proper as is raises no new issues and puts this case in condition for allowance.

Information Disclosure Statement

In paragraph 2 of the Office Action, the Examiner has indicated that the IDS filed April 30, 1999 has not been considered since it references documents cited in the grandparent application (Serial No. 08/235,395), which is unavailable. Applicants submit the listed references with this response. Applicants respectfully submit that late submission should not preclude consideration of the listed references.

Claim Rejections under 35 U.S.C. § 112, first paragraph

On pages 3-8 of the Office Action, the Examiner has rejected claims 37-58 under 35 U.S.C. § 112, first paragraph as allegedly not enabled. Initially, the Examiner asserts, *inter alia*, that "there are five components [of the claimed bifunctional fusion protein or conjugate thereof] which are drawn to large classes of possible components, and therefore are very broadly drawn." Office Action page 4.

The Examiner alleges that the claims are overly broad in view of the specification. However, Applicants maintain that the Examiner's comments are not sufficient to establish a *prima facie* case of enablement since a rejection for breadth, by itself, is not proper, based upon law cited in applicants' previous response. However, in further response, applicants herewith amend claims 37 and 58 to specify that the first component comprises a first portion that is one of a specific set of enzymes and the second portion comprises a monoclonal antibody or antigen binding fragment thereof. In this way, the claims recite a particular structure supported by the specification and examples. Thus, Applicants believe that entry of this amendment is proper as it satisfies the Examiner's concerns about the breadth of the claims and thereby places the claims in condition for allowance.

Conclusion

Based on the foregoing, Applicants assert that the pending claims are allowable and respectfully request early notification of the same. The

Examiner is invited to contact the undersigned for any reason related to the furtherance of this case at the telephone number set forth below.

Respectfully submitted,

May 13, 2002

Patricia D. Granados
Registration No. 33,683

Customer No. 26633
HELLER EHRMAN WHITE & MCAULIFFE LLP
1666 K Street, NW, Suite 300
Washington, DC 20006-1228
(202) 912-2142 (telephone)
(202) 912-2020 (telecopier)

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Director is hereby authorized to charge Deposit Account No. 08-1641 for any such fees; and Applicants hereby petition for any needed extension of time.

Marked up Copy of Claims

37. (Amended) A pharmaceutical kit comprising:

(a) a first component comprising a bifunctional fusion glycoprotein or conjugate thereof comprising

(i) at least one first portion [which possesses enzymatic activity] which is an enzyme selected from the group consisting of penicillin G amidase, penicillin V amidase, β-lactamase, alkaline phosphatase, carboxypeptidase G2, carboxypeptidase A, cytosine deaminase, nitroreductase, diaphorase, arylsulfatase, glycosidase, β-glucosidase, and β-glucuronidase; and

(ii) at least one second portion which comprises a monoclonal antibody or an antigen binding fragment thereof [molecular structure] that binds said first component to a tumor-specific antigen on a tumor cell;

wherein said glycoprotein or conjugate thereof comprises at least one carbohydrate complement comprising at least one exposed carbohydrate residue selected from the group consisting of mannose, galactose, N-acetylglucosamine, N-acetyllactose, glucose and fucose; and

(b) a second component comprising a non-toxic prodrug that is subsequently cleaved into a tumor cytotoxic drug by said enzymatic activity of said first component,

wherein said pharmaceutical kit lacks an additional component that affects clearance of said first component and wherein each of said first and said second components is in a pharmaceutically acceptable vehicle.

49. (Amended) A kit as claimed in claim [48] 37, wherein said [antibody] **monoclonal antibody** or said antigen binding fragment thereof is [a] humanized [antibody].

51. (Amended) A kit as claimed in claim [50] 37, wherein said monoclonal antibody is the monoclonal antibody BW 431/26 or an antigen binding fragment thereof.

58. (Amended) A method of treating a tumor in a subject, comprising:

(a) administering to said subject in a first step, a first component comprising a bifunctional fusion glycoprotein or conjugate thereof comprising

(i) at least one first portion [which possesses enzymatic activity] which is an enzyme selected from the group consisting of penicillin G amidase, penicillin V amidase, β-lactamase, alkaline phosphatase, carboxypeptidase G2, carboxypeptidase A, cytosine deaminase, nitroreductase, diaphorase, arylsulfatase, glycosidase, β-glucosidase, and β-glucuronidase; and

(ii) at least one second portion which comprises a humanized monoclonal antibody or an antigen binding fragment thereof [molecular structure] that binds said first component to a tumor-specific antigen on a tumor cell;

wherein said glycoprotein or conjugate thereof comprises at least one carbohydrate complement comprising at least one exposed carbohydrate residue selected from the group consisting of mannose, galactose, N-acetylglucosamine, N-acetyllactose, glucose and fucose; and

(b) administering to said subject in a second step, a second component comprising a non-toxic prodrug that is subsequently cleaved into a tumor cytotoxic drug by said enzymatic activity of said first component,

wherein said method excludes the administration of an additional component that affects clearance of said first component and wherein each of said first and said second components is in a pharmaceutically acceptable vehicle.